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=> s mRNA (3a) stabl?
L1 2057 MRNA (3A) STABL?

=> s l1 (3a) sequence?
L2 48 L1 (3A) SEQUENCE?

=> s l2 and (degrad? or decay?)
L3 6 L2 AND (DEGRAD? OR DECAY?)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)

=> d bib abs 1-
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L4 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1999:174778 BIOSIS
DN PREV199900174778
TI The cis acting sequences responsible for the differential ***decay*** of the unstable MFA2 and stable PGK1 transcripts in yeast include the context of the translational start codon.
AU LaGrandeur, Thomas; Parker, Roy (1)
CS (1) Department of Molecular and Cellular Biology, Howard Hughes Medical Institute, University of Arizona, Tucson, AZ, 85721 USA
SO RNA (New York), (March, 1999) Vol. 5, No. 3, pp. 420-433.
ISSN: 1355-8382.
DT Article
LA English
AB A general pathway of mRNA turnover has been described for yeast in which the 3' poly(A) tail is first deadenylated to an oligo(A) length, leading to decapping and subsequent 5'-3' exonucleolytic ***decay*** . The unstable MFA2 mRNA and the stable PGK1 mRNAs both ***decay*** through this pathway, albeit at different rates of deadenylation and decapping. To determine the regions of the mRNAs that are responsible for these differences, we examined the ***decay*** of chimeric mRNAs derived from the 5' untranslated, coding, and 3' untranslated regions of these two mRNAs. These experiments have led to the identification of the features of these mRNAs that lead to their different stabilities. The MFA2 mRNA is unstable solely because its 3' UTR promotes the rates of deadenylation and decapping; all other features of this mRNA are neutral with respect to mRNA ***decay*** rates. The PGK1 ***mRNA*** is ***stable*** because the ***sequence*** context of the PGK1 translation start codon and the coding region function together to stabilize the transcript, whereas the PGK1 3' UTR is neutral with respect to ***decay*** . Importantly, changes in the PGK1 start codon context that destabilized the transcript also reduced its translational efficiency. This observation suggests that the nature of the translation initiation complex modulates the rates of mRNA decapping and ***decay*** .

L4 ANSWER 2 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
AN 95256874 EMBASE
DN 1995256874
TI Expression of the early lymphocyte activation antigen CD69, a C-type lectin, is regulated by mRNA ***degradation*** associated with AU-rich sequence motifs.
AU Santis A.G.; Lopez-Cabrera M.; Sanchez-Madrid F.; Proudfoot N.
CS Servicio de Inmunologia, Hospital de la Princesa, calle Diego de Leon 62,E-28006 Madrid, Spain
SO European Journal of Immunology, (1995) 25/8 (2142-2146).
ISSN: 0014-2980 CODEN: EJIMAF
CY Germany
DT Journal; Article
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB CD69 is the earliest inducible cell surface glycoprotein acquired during lymphoid activation both in vitro and in vivo under physiological conditions and inflammation. This molecule is involved in lymphocyte proliferation, and functions as a signal-transmitting receptor in T and B lymphocytes, NK cells and platelets. Molecular cloning of CD69 cDNA revealed that this antigen is a type-II integral membrane protein with a C-type lectin domain in the extracellular region. The expression time course of CD69 mRNA has previously been reported to be transient, peaking around 3 h after induction in T lymphocytes, and declining to nearly resting levels by 8 h. We describe herein studies on the stability of the CD69 mRNA in phorbol ester-activated T lymphocytes. The level of CD69 mRNA in these cells declined rapidly with a half-life of less than 60 min. This finding is consistent with the presence of several AU-rich sequence motifs in the 3' untranslated region (3'UTR), which have been implicated in the selective destabilization of short-lived mRNA of mammalian cytokines, and proto-oncogenes. We have therefore introduced a fragment of the 3'UTR of the human CD69 cDNA, which contains the AU-rich sequence motifs, into the 3'UTR of the rabbit .beta.-globin gene. This inserted ***sequence*** causes the otherwise ***stable*** .beta.-globin ***mRNA*** to become unstable in vivo. A similar destabilizing effect is observed when the 51-nucleotide AU sequence from the mRNA of the human cytokine granulocyte/macrophage colony-stimulating factor is used as a positive control. Furthermore, the introduction of 194-bp fragment from the CD69 3'UTR containing most of the AU-rich motifs was sufficient to induce the destabilizing effect. We propose that the selective ***degradation*** pathway involved in the regulation of the expression of cytokines and proto-oncogenes is implicated in the rapid ***degradation*** of CD69 mRNA in activated T lymphocytes. This pathway may constitute a general mechanism to regulate the expression of inducible molecules involved in inflammatory processes.

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1978:187992 BIOSIS

DN BA68:489
TI REGULATION OF HEMO GLOBIN SYNTHESIS DURING THE DEVELOPMENT OF THE RED CELL
PART 1.
AU NIENHUIS A W; BENZ E J JR
CS CLIN. HEMATOL. BRANCH, NATL. HEART LUNG BLOOD INST., BETHESDA, MD. 20014, USA.
SO N ENGL J MED, (1977) 297 (24), 1318-1328.
CODEN: NEJMAG. ISSN: 0028-4793.
FS BA; OLD
LA English
AB The mature red cell represents the culmination of complex cellular and molecular events by which the primitive stem cell ultimately becomes committed to the highly selective expression of a few genes. In early erythroid cells, globin genes are among the small fraction of DNA sequences that are available for transcription. Most DNA is inaccessible by virtue of its association with histones to form nucleosomes. Nucleosomes may be found on active genes but these structures may then be altered by histone modification or interaction with specific nonhistone chromosomal proteins such that the associated DNA sequences can act as a template for RNA polymerase. Relative rates of ***degradation*** , as well as transcriptional and processing events, may contribute to the accumulation of either total globin mRNA or the mRNA's for individual globins. There may be such intrinsic differences in the primary structures of RNA molecules containing .beta. or .DELTA. mRNA ***sequences*** that .DELTA. ***mRNA*** is relatively less ***stable*** and disappears before erythroid maturation is complete.

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L1 2057 S MRNA (3A) STABL?
L2 48 S L1 (3A) SEQUENCE?
L3 6 S L2 AND (DEGRAD? OR DECAY?)
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L5 23 DUP REM L2 (25 DUPLICATES REMOVED)

=> s l5 not l4
L6 20 L5 NOT L4

=> d bib abs 1-
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L6 ANSWER 1 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:326894 BIOSIS
DN PREV200100326894
TI Amplification of extracellular matrix and oncogenes in tat-transfected human salivary gland cell lines with expression of laminin, fibronectin, collagens I, III, IV, c-myc and p53.
AU McArthur, Carole P. (1); Wang, Yan; Heruth, Daniel; Gustafson, Steven
CS (1) Department of Oral Biology, School of Dentistry, University of Missouri-Kansas City, 650 E 25th Street, Kansas City, MO, 64108: mcarthurc@umkc.edu USA
SO Archives of Oral Biology, (June, 2001) Vol. 46, No. 6, pp. 545-555. print.
ISSN: 0003-9969.
DT Article
LA English
SL English
AB Considerable progress has been made in the transfer of foreign genes into salivary glands in vivo using adenovirus vectors in rats. In an attempt to avoid the transient expression inherent, when using these vectors, retroviral vectors and human cell lines where used here in attempt to develop an in vitro model of HIV-associated salivary gland disease. The HIV-1-tat protein is increasingly implicated in the pathogenesis of the AIDS through altering the expression of strategic cellular genes. The purpose of this study was to transfect human salivary gland (HSG) cell lines in vitro, with the pHIV-1/LTR-tat plasmid, and examine the effect of tat on expression of matrix and basement membrane genes known to be important in the pathogenesis of salivary gland disease. HSG cells were transfected with HIV-1-tat plasmid by the lipofection method. Transfection was confirmed by polymerase chain reaction (PCR) and Southern blot, which verified that tat-specific DNA was present. Tat-mRNA was analysed by Northern blotting and quantified by reverse transcriptase polymerase chain reaction (RT-PCR) to demonstrate its expression. Numerous clones were found to contain integrated tat DNA ***sequences*** and analysis of ***mRNA*** showed ***stable*** expression of tat-specific RNA. Further analysis of mRNA expression for various marker proteins important in HIV pathogenesis showed that the HSG cell line transfected with HIV-1-tat, was associated with significant induction of mRNA expression for extracellular matrix protein. Tat-amplified transcription of the major basement membrane protein laminin, as well as of fibronectin, collagen I and III, and c-myc oncogene was demonstrated. Conversely, expression of p53 suppressor gene mRNA was reduced. Post-transfection expression of collagen IV was erratic and inconclusive. It was concluded that the presence of HIV-tat in this in vitro model of salivary ductal epithelial cell model alters the mRNA expression of several matrix, basement membrane and oncoproteins known to be involved in HIV. pathogenesis. These cell lines provide a useful system for studying the role of tat in the immunopathogenesis of HIV-associated salivary gland disease.

L6 ANSWER 2 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:339979 BIOSIS
DN PREV200000339979
TI Post-transcriptional regulation of urokinase mRNA: Identification of a novel urokinase mRNA-binding protein in human lung epithelial cells in vitro.
AU Shetty, Sreerama (1); Idell, Steven
CS (1) Dept. of Specialty Care Services, University of Texas Health Center at Tyler, 11937 U.S. Highway 271, Tyler, TX, 75708 USA
SO Journal of Biological Chemistry, (May 5, 2000) Vol. 275, No. 18, pp. 13771-13779. print.
ISSN: 0021-9258.
DT Article
LA English
SL English
AB We sought to determine if urokinase expression is regulated at the post-transcriptional level in cultured lung epithelial cells. We also sought to determine if differences in urokinase expression by cultured human lung carcinoma and non-malignant lung epithelial subtypes were attributable to post-transcriptional regulatory mechanisms. Urokinase was expressed by phenotypically diverse lung carcinoma cell lines as well as non-malignant small airway epithelial cells and bronchial epithelial cells. Using gel mobility shift and UV cross-linking assays, we identified a 30-kDa urokinase mRNA-binding protein that selectively bound to a 66-nucleotide protein-binding fragment of urokinase mRNA. The urokinase mRNA-binding protein is found in the cytosolic but not nuclear extracts of non-malignant lung epithelial cells; whereas, it is found in the nuclear but not cytosolic extracts of selected malignant carcinoma-derived cells that express relatively large amounts of urokinase. Chimeric beta-globin/urokinase cDNA containing the urokinase mRNA-binding protein binding ***sequence*** destabilized otherwise ***stable*** beta-globin ***mRNA*** . Our results demonstrate that urokinase gene expression in lung epithelial and lung carcinoma-derived cells is regulated at the post-transcriptional level. The mechanism involves an interaction between a 66-nucleotide sequence of the urokinase mRNA 3'-untranslated region with a newly recognized urokinase mRNA-binding protein to regulate urokinase mRNA stability.

L6 ANSWER 3 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:366331 BIOSIS
DN PREV199799658264
TI Enhanced stability of urokinase-type plasminogen activator mRNA in metastatic breast cancer MDA-MB-231 cells and LLC-PK-1 cells down-regulated for protein kinase C. Correlation with cytoplasmic heterogeneous nuclear ribonucleoprotein C.
AU Nanbu, Rika; Montero, Lilian; D'Orazio, Daniel; Nagamine, Yoshikuni (1)
CS (1) Friedrich Miescher Inst., P.O. Box 2543, CH-4002 Basel Switzerland
SO European Journal of Biochemistry, (1997) Vol. 247, No. 1, pp. 169-174.
ISSN: 0014-2956.
DT Article
LA English
AB In LLC-PK-1 cells, urokinase-type plasminogen activator (uPA) mRNA has a short half-life of 70 min. We have previously demonstrated that most of the regulatory regions responsible for the rapid turnover of uPA mRNA in LLC-PK, cells reside in its 3' untranslated region (3' UTR), where there are at least three regulatory sites, one of which is A + U-rich. This A + U-rich sequence mediates uPA mRNA stabilization induced by protein kinase C (PKC) down-regulation. In this work, we found that uPA mRNA is rather stable in MDA-MB-231 cells with a half-life of 17 h. We compared the stability of hybrid globin mRNA containing different parts of uPA mRNA in its 3' UTR and found that the A + U-rich ***sequence*** of uPA ***mRNA*** renders otherwise ***stable*** globin mRNA unstable in LLC-PK-1 cells but not in MDA-MB-231 cells. We identified a cytoplasmic protein of 40 kDa (p40) which specifically interacts with the A + U-rich sequence. Levels of p40 activity as detected by ultraviolet cross-linking were higher in MDA-MB231 and PKC-down-regulated LLC-PK-1 cells than in untreated LLC-PK-1 cells. Prior treatment of the cytoplasm with a specific antibody against heterogeneous nuclear ribonucteoprotein C (hnRNP C) significantly reduced p40 activity. These results suggest a correlation between the A+U-rich sequence-dependent uPA mRNA stabilization in vivo and the binding of hnRNP C to the A + U-rich sequence in vitro.

L6 ANSWER 4 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:432372 BIOSIS
DN PREV199396086997
TI Leader-mRNA junction sequences are unique for each subgenomic mRNA species in the bovine coronavirus and remain so throughout persistent infection.
AU Hofmann, Martin A.; Chang, Ruey-Yi; Ku, Seulah; Brian, David A. (1)
CS (1) Dep. Microbiol., Univ. Tenn., Knoxville, TN 37996-0845 USA
SO Virology, (1993) Vol. 196, No. 1, pp. 163-171.
ISSN: 0042-6822.
DT Article
LA English

AB The common leader sequence on bovine coronavirus subgenomic mRNAs and
genome was determined. To examine leader-mRNA junction sequences on subgenomic mRNAs, specific oligodeoxynucleotide sets were used in a polymerase chain reaction to amplify junction sequences from either the positive-strand mRNA (eight of nine total identified species) or the negative-strand anti-mRNA (six of the nine species), and sequenced. The mRNA species studied were those for the N, M, S, and HE structural proteins and the 9.5-, 12.7-, 4.8-, and 4.9-kDa putative nonstructural proteins. By defining the leader-mRNA junction sequence as the sequence between (i) the point of mismatch between the leader and genome and (ii) the 3' end of the consensus heptameric intergenic sequence ((U/A)C(U/C)AAAC)), or its variant, a unique junction sequence was found for each subgenomic mRNA species studied. In one instance (mRNA for the 12.7-kDa protein) the predicted intergenic sequence UCCAAAC was not part of the junction region, and in its place was the nonconforming sequence GGTAGAC that occurs just 15 nt downstream in the genome. Leader-mRNA junction sequences found after 296 days of persistent infection were the same as those found during acute infection ( lt 18 hr postinfection). These data indicate that, in contrast to the closely related mouse hepatitis virus, the bovine coronavirus maintains a ***stable*** leader- ***mRNA*** junction ***sequence*** for each mRNA. Interestingly, this stability may be related to the fact that a UCUAA sequence element, postulated by others to be a regulator of the leader-mRNA fusion event, occurs only once within the 3' flanking sequence of the genomic leader donor and once at intergenic sites in the bovine coronavirus genome, whereas it occurs two to four times at these sites in the mouse hepatitis coronavirus.

L6 ANSWER 5 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:117629 BIOSIS
DN PREV199395061729
TI Polypyrimidine tract binding protein interactions with sequences involved in alternative splicing of beta-tropomyosin pre-mRNA.
AU Mulligan, George J.; Guo, Wei; Wormsley, Steven; Helfman, David M. (1)
CS (1) Cold Spring Harbor Lab., P.O. Box 100, Cold Spring Harbor, N.Y. 11724
SO Journal of Biological Chemistry, (1992) Vol. 267, No. 35, pp. 25480-25487. ISSN: 0021-9258.
DT Article
LA English
AB Previous studies of alternative splicing of the rat beta-tropomyosin gene have shown that nonmuscle cells contain factors that block the use of the skeletal muscle exon 7 (Guo, W., Mulligan, G. J., Wormsley, S., and Helfman, D. M. (1991) Genes & Dev. 5, 2095-2106). Using an RNA mobility-shift assay we have identified factors in HeLa cell nuclear extracts that specifically interact with sequences responsible for exon blockage. Here we present the purification to apparent homogeneity of a protein that exhibits these sequence specific RNA binding properties. This protein is identical to the polypyrimidine tract binding protein (PTB) which other studies have suggested is involved in the recognition and efficient use of 3'-splice sites. PTB binds to two distinct functional elements within intron 6 of the beta-tropomyosin pre-mRNA: 1) the polypyrimidine tract sequences required for the use of branch points associated with the splicing of exon 7, and 2) the intron regulatory element that is involved in the repression of exon 7. Our results demonstrate that the sequence requirements for PTB binding are different than previously reported and shows that PTB binding cannot be predicted solely on the basis of pyrimidine content. In addition, PTB fails to bind stably to sequences within intron 5 and intron 7 of beta-TM pre-***mRNA*** , yet forms a ***stable*** complex with ***sequences*** in intron 6, which is not normally spliced in HeLa cells in vitro and in vivo. The nature of the interactions of PTB within this regulated intron reveals several new details about the binding specificity of PTB and suggests that PTB does not function exclusively in a positive manner in the recognition and use of 3'-splice sites.

L6 ANSWER 6 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1992:303987 BIOSIS
DN BA94:17137
TI THE COXII GENE IN CARROT MITOCHONDRIA CONTAINS TWO INTRONS.
AU LIPPOK B; BRENNICKE A; WISSINGER B
CS INSTITUT FUER GENBIOLOGISCHE FORSCHUNG, IHNESTRASSE 63, W-1000 BERLIN 33,
GER.
SO MOL GEN GENET, (1992) 232 (2), 322-327.
CODEN: MGGEAE. ISSN: 0026-8925.
FS BA; OLD
LA English
AB The gene for cytochrome oxidase subunit II (coxII) in carrot is encoded by a unique locus in the mitochondrial genome. In contrast to the coxII genes in the numerous other plant species investigated to date, the coding region is interrupted by two group II introns. The carrot 5' intron is the homologue of the single intervening sequence found in several monocot and dicot coxII genes. Sequences similar to the 3' intron of the carrot coxII gene have not ben reported previously and are not detectable by hybridization with Oenothera mtDNA. Northern hybridizations indicate complex precursor transcript patterns with mRNA molecules up to 10 kb length. The excised intron ***sequences*** appear to be ***stably*** maintained in the ***mRNA*** pool. Amino acid ***sequence*** comparisons suggest that the carrot coxII mRNA needs to be edited by numerous C to U transitions.

L6 ANSWER 7 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:341060 BIOSIS
DN BA92:40435
TI SYNTHESIS ANNEALING PROPERTIES FLUORINE-19 NMR CHARACTERIZATION AND
DETECTION LIMITS OF A TRIFLUOROTHYMIDINE-LABELED ANTISENSE OLIGODEOXYRIBONUCLEOTIDE 21 MER.
AU GMEINER W H; PON R T; LOWN J W
CS DEP. CHEMISTRY, UNIVERSITY ALBERTA, EDMONTON, ALBERTA, CAN. T6G 2G2, CAN.
SO J ORG CHEM, (1991) 56 (11), 3602-3608.
CODEN: JOCEAH. ISSN: 0022-3263.
FS BA; OLD
LA English
AB The synthesis and characterization are described of trifluorothymidine groups incorporated into an antisense 21 mer designed to target gene encode serine proteases in T-lymphocytes. 1H NMR titration studies on 3',5'-O-TPDS-trifluorothymidine (3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)trifluorothymidine) with 3',5'-O-TPDS-2'-deoxyadenosine provided clear evidence of normal Watson-Crick base pairing via detection of the imino proton signals. The chemical shift of the imino proton is moved ca. 0.5 ppm upfield relative to the position with the natural nucleoside. 1H NMR also confirmed normal annealing in the 21 mer with its complement in the imino proton detection with the most notable difference being that six AT signals move upfield into the region characteristic of Watson-Crick GC base pairs. 1D-NMR experiments confirm that a single species exists in solution and CD studies indicate that the duplex formed with its complement adopts B-form geometry. The 1D-NMR experiments show that two of three ordinary methyl groups in the hybrid duplex exist in single conformation while the third methyl group is predominantly in a single conformation. Molecular modeling of the duplex formed between the trifluorothymidine antisense ***sequence*** and complementary ***mRNA*** indicates a ***stable*** A-type helix in the which the CF3 groups cause the thymidine base pairs to be displaced somewhat compared with natural structure. The limits of 19F NMR detection of the trifluorothymidine labeled 21 mer were determined to be ca. 10 .mu.M at a 10:1 signal to noise ratio, i.e., satisfactory for projected in vivo NMR imaging studies.

L6 ANSWER 8 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:271862 BIOSIS
DN BA92:4477
TI MOLECULAR ANALYSES OF TWO POLYADENINE SITE-PROCESSING FACTORS THAT
DETERMINE THE RECOGNITION AND EFFICIENCY OF CLEAVAGE OF THE PRE-MESSENGER
RNA.
AU GILMARTIN G M; NEVINS J R
CS HOWARD HUGHES MED. INST., SECTION GENETICS, DEP. MICROBIOL. IMMUNOL., DUKE
UNIV. MED. CENT., DURHAM, N.C. 27710.
SO MOL CELL BIOL, (1991) 11 (5), 2432-2438.
CODEN: MCEBD4. ISSN: 0270-7306.
FS BA; OLD
LA English
AB Poly(A) site processing of a pre-mRNA requires the participation of multiple nuclear factors. Two of these factors recognize specific ***sequences*** in the pre- ***mRNA*** and form a ***stable*** processing complex. Since these initial interactions are likely critical for the recognition of the poly(A) site and the efficiency of poly(A) site use, we have characterized these factors and the nature of their interaction with the pre-mRNA. The AAUAAA specificity factor PF2 is a large, multicomponent complex composed of at least five distinct polypeptides ranging in molecular size from 170 to 42 kDa. The 170-kDa polypeptide appears to mediate interaction with the pre-mRNA. Factor CF1, which provides specificity for the downstream G+U-rich element and stabilizes the PF2 interaction on the RNA, is also a multicomponent complex but is less complex than PF2. CF1 is composed of three polypeptides of molecular sizes, 76, 64, and 48 kDa. UV cross-linking assays demonstrate that the 64-kDa polypeptide makes direct contact with the RNA, dependent on the G+U-rich downsream sequence element. Moreover, it is clear that these RNA-protein interactions are influenced by the apparent cooperative interaction involving PF2 and CF1, interactions that contribute to the efficiency of poly(A) site processing.

L6 ANSWER 9 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1988:28127 BIOSIS
DN BA85:15852
TI DNA INVERSION WITHIN THE APOLIPOPROTEINS AI-CIII-AIV-ENCODING GENE CLUSTER
OF CERTAIN PATIENTS WITH PREMATURE ATHEROSCLEROSIS.
AU KARATHANASIS S K; FERRIS E; HADDAD I A
CS LAB. MOL. CELL. CARDIOL., DEP. CARDIOL., CHILD. HOSP., BOSTON, MASS.
02115, USA.
SO PROC NATL ACAD SCI U S A, (1987) 84 (20), 7198-7202.
CODEN: PNASA6. ISSN: 0027-8424.
FS BA; OLD
LA English

AB The genes coding for apolipoproteins (apo) AI, CIII, and AIV, designated APOA1, APOC3, and APOA4, respectively, are closely linked and tandemly organized in the long arm of the human chromosome 11. A DNA rearrangement involving the genes encoding apoAI and apoCIII in certain patients with premature atherosclerosis has been associated with deficiency of both apoAI and apoCIII in the plasma of these patients. Structural characterization of the genes for apoAI and apoCIII in one of these patients indicates that this rearrangement consists of a DNA inversion containing portions of the 3' ends of the apoAI and apoCIII genes, including the DNA region between these genes. The breakpoints of this DNA inversion are located within the fourth exon of the apoAI gene and the first intron of the apoCIII gene. Thus, this DNA inversion results in reciprocal fusion of the apoAI and apoCIII gene transcriptional units. Expression of these gene fusions in cultured mammalian cells results in ***stable*** ***mRNA*** transcripts with ***sequences*** representing fusions of the apoAI and apoCIII mRNAs. These results indicate that absence of transcripts with correct apoAI and apoCIII mRNA sequences causes apoAI and apoCIII deficiency in the plasma of these patients and suggest that these apolipoproteins are involved in cholesterol homeostasis and protection against premature atherosclerosis.

L6 ANSWER 10 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1984:322788 BIOSIS
DN BA78:59268
TI DEXAMETHASONE INCREASES THE NUMBER OF RNA POLYMERASE II MOLECULES
TRANSCRIBING INTEGRATED MOUSE MAMMARY TUMOR VIRUS DNA AND FLANKING MOUSE
SEQUENCES.
AU FIRZLAFF J M; DIGGELMANN H
CS SWISS INST. EXP. CANCER RES., 1066 EPALINGES, SWITZ.
SO MOL CELL BIOL, (1984) 4 (6), 1057-1062.
CODEN: MCEBD4. ISSN: 0270-7306.
FS BA; OLD
LA English
AB In mouse Ltk- cells that were transfected with recombinant bacteriophage DNA containing a complete proviral copy of an integrated endogenous mouse mammary tumor virus (MMTV) with its flanking cellular sequences, the newly acquired MMTV proviruses were transcribed in a glucocorticoid-responsive fashion. After hormone treatment of selected cell clones in culture the nuclei were isolated, the nascent RNA chains elongated in vitro, and the number of RNA polymerase II molecules determined on the transcribed MMTV DNA as well as on the flanking mouse DNA sequences. The specific increase in the polymerase loading after hormone treatment is proportional to the increase in the amount of ***stable*** MMTV ***mRNA*** . When the DNA ***sequences*** which are responsible for hormone-receptor binding and for the increased MMTV mRNA levels were deleted, no increase in RNA polymerase II loading on MMTV DNA was observed. Nuclear RNA chains which were transcribed in response to hormone treatment were detected not only from the transfected MMTV DNA but also from the mouse DNA sequences adjacent to the 3' end of the provirus.

L6 ANSWER 11 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1982:208121 BIOSIS
DN BA73:68105
TI REGULATION OF THE S-10 RIBOSOMAL PROTEIN OPERON IN ESCHERICHIA-COLI
NUCLEOTIDE SEQUENCE AT THE START OF THE OPERON.
AU OLINS P O; NOMURA M
CS INSTITUTE FOR ENZYME RESEARCH, UNIV. OF WISCONSIN, MADISON, WIS. 53706.
SO CELL, (1981) 26 (2 PART 2), 205-212.
CODEN: CELLB5. ISSN: 0092-8674.
FS BA; OLD
LA English
AB The DNA sequence of a 1250 base pair segment of the E. coli chromosome that carries the promoter for the S10 ribosomal protein operon, the S10 gene and part of the L3 gene was determined. A DNA fragment carrying the putative S10 promoter was cloned into the plasmid mini-Col E1, which contains a transcription signal close to the single HindII site. Cells harboring the hybrid plasmid produced a relatively ***stable*** hybrid ***mRNA*** with the expected ***sequence*** , demonstrating that the promoter functions in vivo. Comparison of the mRNA sequence around the start of the S10 coding region, the presumed target site for L4 repressor protein, with the known binding site for L4 on 23S rRNA has revealed the presence of sequence homologies. This supports the model of the translational feedback regulation of the S10 operon by L4.

L6 ANSWER 12 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1978:199914 BIOSIS
DN BA66:12411
TI ON THE SECONDARY STRUCTURE IN MESSENGER RNA.
AU KALLENBACH N R
CS DEP. BIOL., UNIV. PA., PHILADELPHIA, PA. 19104, USA.
SO BIOSYSTEMS, (1977 (RECD 1978)) 9 (4), 201-210.
CODEN: BSYMBO. ISSN: 0303-2647.
FS BA; OLD
LA English
AB The sequence present in DNA phase transcripts were investigated by Niyogi using a technique in which mRNA is enzymatically digested to yield different size classes that are resolved chromatographically into populations of equal chain lengths. These chains exhibit specific hybridization to their complementary DNA molecules for lengths N .gtoreq. 10 bases. The stability of the hybrids as a function of temperature was measured experimentally and is analyzed theoretically here by a model which treats the hybrids as ensembles of oligomeric DNA-RNA helices of different chain length and random base sequence. Base pairs with G and C residues (rC .cntdot. dG, rG .cntdot. dC) are assigned a mean enthalpy and entropy of formation distinct from pairs with A and U or T. The theoretical results predict less sensitivity of the stability of the hybrids to G + C mole fraction than is measured. This behavior is consistent with the presence in longer ***mRNA*** fragments of exceptionally ***stable*** ***sequences*** due to clustering of G .cntdot. C pairs or purine vs. pyrimidine configurations on each strand, or both. The existence of stable hairpin secondary structural configurations in the mRNA of bacteriophages T2, T5 and T7 explains this in a natural way, suggesting that these mRNA unconstrained by packing structural requirements such as may hold in RNA phase molecules, also possess a significnt non-random secondary structure.

L6 ANSWER 13 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1978:152176 BIOSIS
DN BA65:39176
TI AN ALTERED SUBUNIT CONFIGURATION ASSOCIATED WITH THE ACTIVELY TRANSCRIBED
DNA OF INTEGRATED ADENOVIRUS GENES.
AU FLINT S J; WEINTRAUB H M
CS DEP. BIOCHEM. SCI., PRINCETON UNIV., PRINCETON, N.J. 08540, USA.
SO CELL, (1977) 12 (3), 783-794.
CODEN: CELLB5. ISSN: 0092-8674.
FS BA; OLD
LA English
AB The sensitivity of DNase I of integrated adenovirus genes that encode mRNA was compared to the sensitivity of adjacent viral DNA sequences that are not expressed as mRNA in 2 lines of adenovirus type 5-transformed hamster cells. The concentrations of integrated DNA sequences homologous to different regions of the viral genome before and after mild DNase I digestion of intact nuclei by measuring the rate of reassociation of restriction endonuclease [Eco RI, Hpa I, Sma I] fragments of labeled adenovirus DNA in the presence of DNA isolated from untreated and digested transformed cell nuclei. The HT14A cell line contains 2.4 copies of the left-hand 35% of the adenovirus type 5 genome per diploid quantity of cell DNA. Integrated sequences that are preferentially sensitive to DNase I include all those encoding mRNA and some additional sequences, equivalent to 3-4 nucleosomes, to the 5' side of the stable mRNA transcript. Thus there is a striking correspondence, to within 3-4 nucleosomes, between the structure of an active transcription unit and the ***stable*** ***mRNA*** ***sequences*** encoded by it. The 2nd cell line examined, HT14B, contains 5.5 copies of the left-hand 40% of the adenovirus type 5 genome per diploid quantity of cell DNA. Of the sequences complementary to viral mRNA, only half are preferentially sensitive to DNase I. By contrast, the majority of the integrated viral DNA sequences that are not expressed as mRNA are resistant to DNase I digestion in this and the HT14A cell line. The results observed with HT14B cells suggest that only half of the integrated adenovirus sequences are in a chromatin conformation that permits transcription to occur.

L6 ANSWER 14 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1977:216000 BIOSIS
DN BA64:38364
TI TRANSCRIPTION OF THE GENOME OF ADENOVIRUS TYPE 12 PART 4 MAPS OF STABLE
LATE RNA FROM PRODUCTIVELY INFECTED HUMAN CELLS.
AU SCHEIDTMANN K-H; DOERFLER W
SO J VIROL, (1977) 22 (3), 585-590.
CODEN: JOVIAM. ISSN: 0022-538X.
FS BA; OLD
LA Unavailable
AB From human [oral carcinoma] KB cells productively infected with adenovirus type 12, mRNA and stable nuclear RNA were isolated late (42 h) after infection. Using restriction endonuclease [EcoRI and BamHI] fragments of adenovirus type 12 DNA, ***mRNA*** and ***stable*** nuclear RNA ***sequences*** were mapped on the viral genome. Late after infection, preferentially the r (= rightward) strand is transcribed into stable nuclear RNA, but the l (= leftward) strand is expressed only to a minor extent. Adenovirus type 12-specific mRNA originates from the following sections on the viral genome: 0-0.11, 0.18-0.20, 0.27-0.49, 0.56-0.63, 0.68-0.84 and 0.89-0.92 fractional length units on the r strand and 0.11-0.16, 0.22-0.27, 0.50-0.54, 0.62-0.66, 0.855-0.865 and 0.93-1.0 fractional length units on the l strand. Self-complementary viral RNA isolated at 8 h postinfection is complementary to about 20% of each strand of the viral genome, and self-complementary viral RNA isolated at 42 h postinfection anneals to 70-80% of each strand of the viral genome.

L6 ANSWER 15 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 82120214 EMBASE
DN 1982120214
TI Temporal patterns of human cytomegalovirus transcription: Mapping the viral RNAs synthesized at immediate early, early, and late times after infection.
AU Wathen M.W.; Stinski M.F.

CS Dept. Microbiol., Univ. Iowa, Iowa City, IA 52242, United States
SO Journal of Virology, (1982) 41/2 (462-477).
CODEN: JOVIAM
CY United States
DT Journal
FS 047 Virology
022 Human Genetics
LA English
AB The transcription of the human cytomegalovirus genome was investigated at immediate early, early, and late times after infection. Viral RNAs associated with either the whole cell, the nucleus, the cytoplasm, or the polyribosomes were analyzed. At immediate times, i.e., in the absence of de novo viral protein synthesis, the viral RNA in high abundance originated from a region of the long unique section of the prototype arrangement of the viral genome (0.660 to 0.770 map units). The viral RNA in low abundance originated from the long repeat sequences (0.010 to 0.035 and 0.795 to 0.825 map units) and a region in the long unique section (0.021 to 0.260 map units). Viral RNAs associated with the polyribosomes as polyadenylated RNA were mapped to these restricted regions of the viral genome and characterized according to size class in kilobases. At 24 h after infection in the presence of an inhibitor of viral DNA replication, i.e., at early times, the stable viral RNAs in highest abundance mapped in the long repeat sequences. Viral RNAs at intermediate abundance under these conditions mapped in two regions of the long unique section of the viral genome (0.325 to 0.460 and 0.685 to 0.770 map units). Stable viral RNAs that were associated with the polyribosomes in high abundance as polyadenylated RNA originated from the long repeat sequences, but not from the long unique section of the viral genome. An analysis of whole-cell RNA at late times (72 h) indicated that the abundant transcription was in the regions of the long unique sequences (0.325 to 0.460 and 0.660 to 0.685 map units), and transcription of intermediate abundance was from the long repeat ***sequences*** . However, ***stable*** viral ***mRNA*** 's derived from the long repeat sequences were associated with the polyribosomes at late times after infection. In addition, mRNA's originating from the long and short unique sequences were found associated with the polyribosomes at higher relative concentration that at early times after infection. It is proposed that expression of the immediate early viral genes is required to transcribe the early viral genes in the long repeat and adjacent sequences. These sequences are also transcribed at late times after infection while viral DNA synthesis continues. The expression of viral genes in most of the long and short unique sequences appears to require viral DNA replication.

L6 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 2002:603213 CAPLUS
TI Molecular characterization of long direct repeat (LDR) ***sequences*** expressing a ***stable*** ***mRNA*** encoding for a 35-amino-acid cell-killing peptide and a cis-encoded small antisense RNA in Escherichia coli
AU Kawano, Mitsuoki; Oshima, Taku; Kasai, Hiroaki; Mori, Hirotada
CS Research and Education Center for Genetic Information, Nara Institute of Science and Technology, Nara, 630-0101, Japan
SO Molecular Microbiology (2002), 45(2), 333-349
CODEN: MOMIEE; ISSN: 0950-382X
PB Blackwell Science Ltd.
DT Journal
LA English
AB Genome sequence analyses of Escherichia coli K-12 revealed four copies of long repetitive elements. These sequences are designated as long direct repeat (LDR) sequences. Three of the repeats (LDR-A, -B, -C), each approx. 500bp in length, are located as tandem repeats at 27.4 min on the genetic map. Another copy (LDR-D), 450bp in length and nearly identical to LDR-A, -B and -C, is located at 79.7 min, a position that is directly opposite the position of LDR-A, -B and -C. In this study, we demonstrate that LDR-D encodes a 35-amino-acid peptide, LdrD, the overexpression of which causes rapid cell killing and nucleoid condensation of the host cell. Northern blot and primer extension anal. showed constitutive transcription of a stable mRNA (.apprxeq. 370 nucleotides) encoding LdrD and an unstable cis-encoded antisense RNA (.apprxeq. 60 nucleotides), which functions as a trans-acting regulator of ldrD translation. We propose that LDR encodes a toxin-antitoxin module. LDR-homologous sequences are not present on any known plasmids but are conserved in Salmonella and other enterobacterial species.

L6 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1995:998153 CAPLUS
DN 124:47638
TI Increased cytokine or protooncogene protein expression by transfected cell using mutants with altered affinity for mRNA AU-binding factor
IN Malter, James S.
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9529244 | A1 | 19951102 | WO 1995-US4903 | 19950421 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5587300 | A | 19961224 | US 1994-233130 | 19940426 |
| AU 9522959 | A1 | 19951116 | AU 1995-22959 | 19950421 |
| PRAI US 1994-233130 | | 19940426 | | |
| WO 1995-US4903 | | 19950421 | | |

AB The present invention provides a method to increase the prodn. of a regulatory mol., i.e., a mol. that regulates cell behavior, such as a cytokine or a protooncogene, in population of transfected cells, whether normal (resting or activated) or tumor cells. The method involves mutating a native or "wild type" cDNA sequence that encodes an mRNA sequence for a regulatory mol. to form a mutant cDNA sequence capable of producing a more ***stable*** ***mRNA*** ***sequence*** . Specifically, the method involves mutating a wild type cDNA sequence that encodes an unstable mRNA sequence for the regulatory mol., wherein the mRNA includes a 3' untranslated region having a destabilizing element comprising an AUUUA sequence, to form a mutant cDNA sequence capable of producing a more ***stable*** ***mRNA*** ***sequence*** , wherein the AUUUA sequence is replaced by AUGUA, AUAUA, GUGUG, AGGGA, GAGAG, or a combination thereof; and transfecting a cell population with the mutant cDNA sequence so that the prodn. of the regulatory mol. is enhanced by the cells.

L6 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1995:141046 CAPLUS
DN 122:2496
TI Occurrence of a LINE sequence in the 3' UTR of the goat .alpha.s1-casein E- encoding allele associated with reduced protein synthesis level
AU Jansa Perez, Marta; Leroux, Christine; Sanchez Bonastre, Armand; Martin, Patrice
CS Laboratoire de Genetique biochimique et de Cytogenetique, Institut National de la Recherche Agronomique, 78352, Jouy-en-Josas, Fr.
SO Gene (1994), 147(2), 179-87
CODEN: GENED6; ISSN: 0378-1119
PB Elsevier
DT Journal
LA English
AB The E allele of the .alpha.s1-casein (.alpha.s1-Cas)-encoding gene is assocd. with a reduced casein content in milk. Structural anal. of mRNA and sequencing of amplified genomic DNA fragments, have revealed that this allele contains a 457-bp insertion within exon 19 (last untranslated exon). This insert is a truncated long interspersed repeated element (LINE) contg. part of the ORF-2, the 3' UTR and the poly(A) tail of the original retroposon. This LINE sequence was found to be highly repeated in the goat genome. The threefold redn. in the amt. of .alpha.s1-CasE mRNA in the total, as well as in the polysomal fractions, as compared with its A counterpart, leads one to suppose either a reduced transcriptional rate of allele E or/and a decreased stability of the relevant mRNA. Northern blot and PCR expts. suggested the setting up of highly stable secondary structures involving the 3' UTR of the .alpha.s1-CasE transcript. The mRNA folding calcns. support such an hypothesis, by base-pairing interactions between the E allele messenger poly(A) tail and a long poly(U)-stretch occurring at the 5' end of the insertion. In addn., since A+U-rich motifs are also present in the truncated LINE insertion, the authors propose that this extra sequence might be responsible for the lower milk .alpha.s1-Cas content by reducing the allele E mRNA stability.

L6 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1988:144732 CAPLUS
DN 108:144732
TI Preparation and expression of a synthetic gene for human epidermal cell growth factor
IN Taniyama, Yoshio; Igarashi, Koichi; Marumoto, Ryuji
PA Takeda Chemical Industries, Ltd., Japan
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 177915 | A2 | 19860416 | EP 1985-112653 | 19851005 |
| EP 177915 | A3 | 19870805 | | |
| EP 177915 | B1 | 19910109 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 61088881 | A2 | 19860507 | JP 1984-210502 | 19841009 |
| JP 06042833 | B4 | 19940608 | | |
| JP 62040290 | A2 | 19870221 | JP 1985-176976 | 19850813 |
| JP 06044866 | B4 | 19940615 | | |
| CA 1263619 | A1 | 19891205 | CA 1985-492430 | 19850908 |
| US 4849350 | A | 19890718 | US 1985-784844 | 19851004 |
| AT 59861 | E | 19910115 | AT 1985-112653 | 19851005 |
| PRAI JP 1984-210502 | | 19841009 | | |
| JP 1985-176976 | | 19850813 | | |
| EP 1985-112653 | | 19851005 | | |

AB A synthetic gene encoding human EGF (hEGF) contains ***sequences*** which produce ***stable*** ***mRNA*** , leading to efficient translation of mRNA and efficient prodn. of hEGF. Thus, pTB506 contains chem. synthesized and enzymically joined coding sequences which are ligated to a SV40 promoter and the LTR region of the Evelson mouse

leukemia virus. The expression plasmid was cotransformed with p40A8 marker (carrying a human hypoxanthine phosphoribosyltransferae [HPRT] cDNA
marker) into mouse HPRT-defective L cells. The transformants produced 1.4 ng of hEGF/107 cells.

L6 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 1986:585264 CAPLUS
DN 105:185264
TI Vectors for high-level gene expression
IN Anderson, David Martin; McQuire, Jeffrey Clark
PA Genex Corp., USA
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 182636 | A2 | 19860528 | EP 1985-308361 | 19851115 |
| EP 182636 | A3 | 19880107 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| US 4798791 | A | 19890117 | US 1984-671967 | 19841116 |
| JP 61158794 | A2 | 19860718 | JP 1985-255151 | 19851115 |
| US 5149657 | A | 19920922 | US 1991-655234 | 19910208 |
| PRAI US 1984-671967 | | 19841116 | | |
| US 1984-650128 | | 19840913 | | |
| US 1986-933945 | | 19861124 | | |
| US 1987-25140 | | 19870312 | | |

AB A method is described for expressing a gene encoding for a desired protein (e.g. prochymosin) in a bacterium (e.g. Escherichia coli) at elevated levels of expression. The steps comprise: (a) ligating a terminal mRNA sequence from a gene coding for a ***stable*** ***mRNA*** ***sequence*** coding for a bacterial protein to the 3'-end of the translation termination codon of a structural gene for the desired protein; (b) inserting the ligated gene in a vector which is replicable in the bacterium such that the gene is operably linked to a transcription promoter; (c) transforming of the bacterium with the vector contg. the gene; and (d) expressing the gene in the transformed bacterium. Thus, an oligopeptide sequence contg. the trpt sequence followed by restriction sites for XbaI, NarI, NeoI and SalI was prepd. by std. methods; the trp promoter (Ptrp) was present at the 3'-end in order to promote transcription of trpED stabilization gene. This synthetic oligonucleotide was ligated to the HpaI restriction site of plasmid pGX2257, which contains the gene for prochymosin, to form the recombinant plasmid pGX2287. It was shown that E. coli transformed with plasmid pGX2287 which contains the trpt sequence immediately downstream from the translation termination signal of the .DELTA.-2-prochymosin gene produced several fold higher titers of chymosin than the parental strain pGX2257.

=> d his

(FILE 'HOME' ENTERED AT 16:54:05 ON 19 AUG 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:54:31 ON 19 AUG 2002
L1 2057 S MRNA (3A) STABL?
L2 48 S L1 (3A) SEQUENCE?
L3 6 S L2 AND (DEGRAD? OR DECAY?)
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 23 DUP REM L2 (25 DUPLICATES REMOVED)
L6 20 S L5 NOT L4

=> s l1 and (radicicol or radicicol analog A)
L7 0 L1 AND (RADICICOL OR RADICICOL ANALOG A)

=> s (radicicol or radicicol analog A)
L8 358 (RADICICOL OR RADICICOL ANALOG A)

=> s l8 and mRNA
L9 27 L8 AND MRNA

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 12 DUP REM L9 (15 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
1
AN 2002:416762 BIOSIS
DN PREV200200416762
TI Critical role for cataplerosis via citrate in glucose-regulated insulin release.
AU Flamez, Daisy; Berger, Veerle; Kruhoffer, Mogens; Orntoft, Torben; Pipeleers, Daniel; Schuit, Frans C. (1)
CS (1) Diabetes Research Center, Vrije Universiteit Brussel, Laarbeeklaan 103, B-1090, Brussels: fschuit@minf.vub.ac.be Belgium
SO Diabetes, (July, 2002) Vol. 51, No. 7, pp. 2018-2024. http://www.diabetes.org/Diabetes/. print.
ISSN: 0012-1797.
DT Article
LA English
AB The molecular mechanisms mediating acute regulation of insulin release by glucose are partially known. The process involves at least two pathways that can be discriminated on basis of their (in)dependence of closure of ATP-sensitive potassium (K+ATP) channels. The mechanism of the K+ATP channel-independent pathway was proposed to involve cataplerosis, the export of mitochondrial intermediates into the cytosol and in the induction of fatty acid-derived signaling molecules. In the present article, we have explored in fluorescence-activated cell sorter (FACS)-purified rat beta-cells the molecular steps involved in chronic glucose regulation of the insulin secretory response. When compared with culture in 10 mmol/l glucose, 24 h culture in 3 mmol/l glucose shifts the phenotype of the cells into a state with low further secretory responsiveness to glucose, lower rates of glucose oxidation, and lower rates of cataplerosis. Microarray ***mRNA*** analysis indicates that this shift can be attributed to differences in expression of genes involved in the K+ATP channel-dependent pathway, in cataplerosis and in fatty acid/cholesterol biosynthesis. This response was paralleled by glucose upregulation of the transcription factor sterol regulatory element binding protein 1c (SREBP1c) (ADD1) and downregulation of peroxisome proliferator-activated receptor (PPAR)-alpha and PPAR-beta (PPARdelta). The functional importance of cataplerosis via citrate for glucose-induced insulin release was further supported by the observation that two ATP-citrate lyase inhibitors, ***radicicol*** and (-)-hydroxy-citrate, block part of glucose-stimulated release in beta-cells. In conclusion, chronic glucose regulation of the glucose-responsive secretory phenotype is associated with coordinated changes in gene expression involved in the K+ATP channel-dependent pathway, in cataplerosis via citrate and in acyl CoA/cholesterol biosynthesis.

L10 ANSWER 2 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
2
AN 2001:469211 BIOSIS
DN PREV200100469211
TI Suppression of IL-8 gene expression by ***radicicol*** is mediated through the inhibition of ERK1/2 and p38 signaling and negative regulation of NF-kappaB and AP-1.
AU Na, Yong Ju; Jeon, Young Jin; Suh, Jae-Hong; Kang, Jong Soon; Yang, Kyu-Hwan; Kim, Hwan-Mook (1)
CS (1) Korea Research Institute of Bioscience and Biotechnology (KRIBB), Yusong, Taejon, 305-600: hwanmook@mail.kribb.re.kr South Korea
SO International Immunopharmacology, (September, 2001) Vol. 1, No. 9-10, pp. 1877-1887. print.
ISSN: 1567-5769.
DT Article
LA English
SL English
AB We show that ***radicicol*** , an anti-fungal agent, inhibits interleukin-8 (IL-8) production by the human monocyte line THP-1 in response to phorbol-12-myristate-13-acetate/lipopolysaccharide (PMA/LPS). IL-8 is a potent chemokine and needs for an optimal immune response-such as inflammation by activation of neutrophils. The decrease in PMA/LPS-induced IL-8 ***mRNA*** expression was demonstrated by quantitative reverse transcription-polymerase chain reaction (RT-PCR). Since the promoter in IL-8 gene contains binding motifs for NF-kappaB, AP-1, and NF-IL6, which appear to be important in IL-8 induction, the effects of ***radicicol*** on the activation of these transcription factors were examined. Treatment of ***radicicol*** to THP-1 cells produced a strong inhibition of NF-kappaB and AP-1, while NF-IL6 was not significantly affected by ***radicicol*** . Western blot analysis showed that ***radicicol*** inhibited the phosphorylation and phosphotransferase activities of extracellular signal-regulated kinases 1 and 2 (ERK1/2) and p38. PD98059 and SB203580, known as a specific inhibitor of MEK1 and p38 kinase, respectively, inhibited IL-8 gene expression showing that both of the kinase pathways are involved in IL-8 regulation in human monocytes. Collectively, this series of experiments indicates that ***radicicol*** inhibits IL-8 gene expression by blocking ERK1/2 and p38 signaling.

L10 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
3
AN 2002:101270 BIOSIS
DN PREV200200101270
TI A ***radicicol*** derivative, KF58333, inhibits expression of hypoxia-inducible factor-1alpha and vascular endothelial growth factor, angiogenesis and growth of human breast cancer xenografts.
AU Kurebayashi, Junichi (1); Otsuki, Takemi; Kurosumi, Masafumi; Soga, Shiro; Akinaga, Shiro; Sonoo, Hiroshi (1)
CS (1) Department of Breast and Thyroid Surgery, Kawasaki Medical School, 577 Matsushima Kurashiki, Okayama, 701-0192: kure@med.kawasaki-m.ac.jp Japan
SO Japanese Journal of Cancer Research, (December, 2001) Vol. 92, No. 12, pp. 1342-1351. print.
ISSN: 0910-5050.
DT Article
LA English
AB A novel oxime derivative of ***radicicol*** , KF58333, binds to the heat shock protein 90 (Hsp90) and destabilizes its associated signaling molecules. These effects play a critical role in the growth inhibition of tumor cells. To further investigate the effects of this agent, it was

administered to two human breast cancer cell lines, KPL-1 and KPL-4, both in vitro and in vivo. KF58333 dose-dependently inhibited the growth and vascular endothelial growth factor (VEGF) secretion, concomitantly with a decrease in VEGF ***mRNA*** expression, in each cell line. This agent also suppressed the increase of VEGF secretion and expression induced by hypoxia (1% O2). Intravenous injections of this agent into nude mice bearing either KPL-1 or KPL-4 xenografts significantly inhibited the tumor growth associated with a decrease in the Ki67 labeling index and microvascular area and an increase in apoptosis and the necrotic area. These findings indicate that the antitumor activity of this ***radicicol*** derivative may be partly mediated by decreasing VEGF secretion from tumor cells and inhibiting tumor angiogenesis. To explore the action mechanisms of the anti-angiogenic effect, the expression level of hypoxia-inducible factor (HIF)-1alpha was investigated. KF58333 provided a significant decrease in the HIF-1alpha protein expression under both normoxic and hypoxic conditions. In contrast, the ***mRNA*** expression of HIF-1alpha was not decreased by this agent. It is suggested that the post-transcriptional down-regulation of HIF-1alpha expression by this agent may result in a decrease of VEGF expression and tumor angiogenesis.

L10 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4
AN 2001:220477 BIOSIS
DN PREV200100220477
TI P2Y2 nucleotide receptor signaling in human monocytic cells: Activation, desensitization, and coupling to mitogen-activated protein kinases.
AU Santiago-Perez, Laura I.; Flores, Rosa V.; Santos-Berrios, Cynthia; Chorna, Nataliya E.; Krugh, Brent; Garrad, Richard C.; Erb, Laurie; Weisman, Gary A.; Gonzalez, Fernando A. (1)
CS (1) Department of Chemistry, University of Puerto Rico, San Juan, 00931-3346: fgonzal@upracd.upr.clu.edu Puerto Rico
SO Journal of Cellular Physiology, (May, 2001) Vol. 187, No. 2, pp. 196-208. print.
ISSN: 0021-9541.
DT Article
LA English
SL English
AB Activation of P2Y2 receptors by extracellular nucleotides has been shown to induce phenotypic differentiation of human promonocytic U937 cells that is associated with the inflammatory response. The P2Y2 receptor agonist, UTP, induced the phosphorylation of the MAP kinases MEK1/2 and ERK1/2 in a sequential manner, since ERK1/2 phosphorylation was abolished by the MEK1/2 inhibitor PD 098059. Other results indicated that P2Y2 receptors can couple to MAP kinases via phosphatidylinositol 3-kinase (PI3K) and c-src. Accordingly, ERK1/2 phosphorylation induced by UTP was inhibited by the PI3K inhibitors, wortmannin and LY294002, and the c-src inhibitors, ***radicicol*** and PP2, but not by inhibitors of protein kinase C (PKC). The phosphorylation of ERK1/2 was independent of the ability of P2Y2 receptors to increase the concentration of intracellular free calcium, since chelation of intracellular calcium by BAPTA did not diminish the phosphorylation of ERK1/2 induced by UTP. A 5-minute treatment with UTP reduced U937 cell responsiveness to a subsequent UTP challenge. UTP-induced desensitization was characterized by an increase in the EC50 for receptor activation (from 0.44 to 9.3 muM) and a dramatic (apprx75%) decrease in the maximal calcium mobilization induced by a supramaximal dose of UTP. Phorbol ester treatment also caused P2Y2 receptor desensitization (EC50 = 12.3 muM UTP and maximal calcium mobilization reduced by apprx33%). The protein kinase C inhibitor GF 109203X failed to significantly inhibit the UTP-induced desensitization of the P2Y2 receptor, whereas the protein phosphatase inhibitor okadaic acid blocked receptor resensitization. Recovery of receptor activity after UTP-induced desensitization was evident in cells treated with agonist for 5 or 30 min. However, P2Y2 receptor activity remained partially desensitized 30 min after pretreatment of cells with UTP for 1 h or longer. This sustained desensitized state correlated with a decrease in P2Y2 receptor ***mRNA*** levels. Desensitization of ERK1/2 phosphorylation was induced by a 5-minute pretreatment with UTP, and cell responsiveness did not return even after a 30-minute incubation of cells in the absence of an agonist. Results suggest that desensitization of the P2Y2 receptor may involve covalent modifications (i.e., receptor phosphorylation) that functionally uncouple the receptor from the calcium signaling pathway, and that transcriptional regulation may play a role in long-term desensitization. Our results indicate that calcium mobilization and ERK1/2 phosphorylation induced by P2Y2 receptor activation are independent events in U937 monocytes.

L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:457226 CAPLUS
DN 133:71088
TI Reporter gene assay for identifying compounds affecting ***mRNA*** stability
IN Kastelic, Tania; Cheneval, Dominique
PA Novation Pharmaceuticals Inc., Can.
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000039314 | A1 | 20000706 | WO 1999-CA1235 | 19991223 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1141358 | A1 | 20011010 | EP 1999-962013 | 19991223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI GB 1998-28709 | A | 19981224 | | |
| WO 1999-CA1235 | W | 19991223 | | |

AB A reporter gene-based assay method is provided for the identification of a compd. which affects ***mRNA*** stability, in particular induces ***mRNA*** degrdn. DNA expression system which in the absence of test compd. capable of expressing a protein having a detectable signal, wherein the ***mRNA*** which codes for the protein transcribed from the expression system comprises at least one copy of a ***mRNA*** instability sequence, is contacted with a test compd. and the detectable signal is measured in the presence of the test compd. and compared with a control. A stably transfected cell line contg. the DNA expression system is claimed. The use of compds. which induce degrdn. of ***mRNA*** , identified by the system for prophylaxis and therapy of diseases or medical conditions related to inappropriate ***mRNA*** stabilization is also claimed. ***Radicicol*** and ***Radicicol*** ***analog*** ***A*** were identified as compds. affecting ***mRNA*** stability in THP-1 cell lines stably transformed with a luciferase reporter gene construct.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:456875 CAPLUS
DN 133:94513
TI Compounds which affect ***mRNA*** stability and uses therefor
IN Kastelic, Tania; Cheneval, Dominique; Ruetz, Stephan
PA Novation Pharmaceuticals Inc., Can.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000038674 | A1 | 20000706 | WO 1999-CA1234 | 19991223 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1140069 | A1 | 20011010 | EP 1999-962012 | 19991223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI GB 1998-28707 | A | 19981224 | | |
| GB 1998-28710 | A | 19981224 | | |
| WO 1999-CA1234 | W | 19991223 | | |

OS MARPAT 133:94513
AB Compds. which induce degrdn. of ***mRNA*** which contains 1 or more ***mRNA*** instability sequences are provided for use as pharmaceuticals, e.g. for use in the prophylaxis or treatment of diseases and medical conditions in general having an etiol. assocd. with the increased or prolonged stability of mRNAs, and which on prolonged or inappropriate expression typically give rise to undesirable effects, e.g., cancer cell growth or an unwanted inflammatory response. Thus, tablets contained a ***radicicol*** analog 500.0, lactose 500.0, potato starch 352.0, gelatin 8.0, talc 60.0, Mg stearate 10.0, EtOH qs and SiO2 20.0 g/10,000 tablets.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5
AN 2000:426201 BIOSIS
DN PREV200000426201
TI ***Radicicol*** suppresses expression of inducible nitric-oxide synthase by blocking p38 kinase and nuclear factor-kappaB/Rel in lipopolysaccharide-stimulated macrophages.
AU Jeon, Young J.; Kim, Young K.; Lee, Michael; Park, Sun M.; Han, Sang B.; Kim, Hwan M. (1)
CS (1) Korea Research Institute of Bioscience and Biotechnology, Yusong, Taejon, 305-600 South Korea
SO Journal of Pharmacology and Experimental Therapeutics, (August, 2000) Vol. 294, No. 2, pp. 548-554. print.
ISSN: 0022-3565.

DT Article
LA English
SL English
AB We show that ***radicicol*** , a fungal antibiotic, produces a marked inhibition of p38 kinase, nuclear factor-kappaB/Rel (NF-kappaB/Rel), and inducible nitric-oxide synthase (iNOS) transcription by the macrophage line RAW 264.7 in response to lipopolysaccharide (LPS). Treatment of RAW 264.7 with ***radicicol*** inhibited LPS-stimulated p38 kinase phosphorylation in a dose-related manner. iNOS transcription, which is regulated in part by the NF-kappaB/Rel family of transcription factors, has been shown to be under the control of the p38 kinase signaling cascade. Our data also show that the p38 kinase pathway is specifically involved in LPS-induced NF-kappaB/Rel activation and iNOS expression because NF-kappaB/Rel DNA binding and iNOS ***mRNA*** production in the presence of a specific inhibitor of p38 kinase, SB203580, were dramatically diminished. In contrast, PD98059, a specific inhibitor of mitogen-activated protein kinase/extracellular signal-regulated protein kinase kinase 1 had no effect on NF-kappaB/Rel activation and iNOS expression. LPS-induced loss of inhibitory proteins IkappaB-alpha and IkappaB-beta and translocation of p65, c-Rel, and p50 was inhibited by ***radicicol*** . Collectively, this series of experiments indicates that ***radicicol*** inhibits iNOS gene expression by blocking p38 kinase signaling. Due to the critical role that NO release plays in mediating inflammatory responses, the inhibitory effects of ***radicicol*** on iNOS suggest that this potent antifungal agent may represent a useful anti-inflammatory agent.

L10 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
6
AN 1999:98552 BIOSIS
DN PREV199900098552
TI v-src Induces cisplatin resistance by increasing the repair of cisplatin-DNA interstrand cross-links in human gallbladder adenocarcinoma cells.
AU Masumoto, Naoko; Nakano, Shuji (1); Fujishima, Hiromitsu; Kohno, Kimitoshi; Niho, Yoshiyuki
CS (1) First Dep. Internal Med., Faculty Med., Kyushu Univ., 3-1-1 Maidashi, Fukuoka, Fukuoka 812 Japan
SO International Journal of Cancer, (March 1, 1999) Vol. 80, No. 5, pp. 731-737.
ISSN: 0020-7136.
DT Article
LA English
AB Activation of Src, which has an intrinsic protein tyrosine kinase (PTK) activity, has been demonstrated in human solid tumors, such as colorectal and breast cancers. To investigate the role of activated Src in drug resistance, we evaluated the effect of v-src on the resistance to various anti-cancer drugs using v-src-transfected HAG-1 human gallbladder adenocarcinoma cells. Compared with parental or mock-transfected HAG-1 cells, v-src-transfected HAG/src3-1 cells showed a 3.5-fold resistance to cis-diamminedichloroplatinum (II) (CDDP) but not to doxorubicin, etoposide or 5-fluorouracil. By contrast, activated H-ras, which acts downstream of src, failed to induce resistance to either of these drugs. Furthermore, wortmannin, a phosphatidylinositol (PI) 3-kinase inhibitor, and H7, a protein kinase C (PKC) inhibitor, did not alter CDDP resistance. Evaluation of the kinetics of the removal of DNA interstrand cross-links (ICLs), measured by alkaline elution, showed a significant increase in this removal in HAG/src3-1 cells as compared with mock-transfected cells, though no differences were found in the formation of DNA ICLs between these cell lines. CDDP resistance in v-src-transfected cells was reversed, if not completely, by either herbimycin A or ***radicicol*** , specific inhibitors of Src-family PTKs, suggesting that Src tyrosine kinase activity induces CDDP resistance. Moreover, significant reduction in the repair of CDDP-induced DNA ICLs was observed upon treatment with ***radicicol*** . The intracellular glutathione content and ***mRNA*** expression of topoisomerase II and metallothionein were virtually identical between these cell lines, except for topoisomerase I ***mRNA*** . Our data strongly suggest that the ability of activated src, but not ras, to induce CDDP resistance is mediated by augmentation of DNA repair through Src to downstream signal-transduction pathways distinct from either the Ras, PI 3-kinase or PKC pathway.

L10 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1998:154166 CAPLUS
DN 128:252691
TI Inhibitor of protein tyrosine kinase, ***radicicol*** , suppresses the expression of cyclooxygenase and pro-inflammatory cytokines in LPS-stimulated rat alveolar macrophage in part by accelerating degradation of ***mRNA***
AU Feng, Lili; Jang, Byeong C.; Hwang, Daniel
CS Department of Immunology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Advances in Experimental Medicine and Biology (1997), 407(Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury 3), 281-288
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Publishing Corp.
DT Journal
LA English
AB The inhibition of TNF.alpha. and IL-1.beta. expression by ***radicicol*** is at least in part do to accelerated decay of ***mRNA*** . ***Radicicol*** also inhibits tyrosine phosphorylation of MAP kinases.

L10 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
7
AN 1997:63730 BIOSIS
DN PREV199799362933
TI Induction of rapid IL-1-beta ***mRNA*** degradation in THP-1 cells mediated through the AU-rich region in the 3'UTR by a ***radicicol*** analogue.
AU Kastelic, Tania; Schnyder, Joerg; Leutwiler, Albert; Traber, Rene; Streit, Bruno; Niggli, Heinz; MacKenzie, Andrew; Cheneval, Dominique (1)
CS (1) Sandoz Res. Inst. Berne, Inflammation, Monbijoustr. 115, CH-3007 Bern Switzerland
SO Cytokine, (1996) Vol. 8, No. 10, pp. 751-761.
ISSN: 1043-4666.
DT Article
LA English
AB A ***radicicol*** analogue (analogue A) was found to inhibit interleukin 1 beta (IL-1-beta) and tumour necrosis factor alpha (TNF-alpha) secretion from THP-1 cells. If added to cells activated by interferon gamma and lipopolysaccharide, ***radicicol*** analogue A not only inhibited the secretion of IL-1-beta but also induced an extremely rapid degradation of IL-1-beta, IL-6 and TNF-alpha ***mRNA*** to undetectable levels within 5-8 h. This degradation is independent of translation and of the signal inducing transcription. The common feature of these genes is the inclusion of one or more copies of the ***mRNA*** -instability sequence, AUUUA, in the 3' untranslated region. Indeed, no destabilizing effect of ***radicicol*** analogue A could be observed on ***mRNA*** derived from the expression of an IL-1-beta construct lacking the AUUUA motifs of the 3'UTR. The effect of ***radicicol*** analogue A on protein/ ***mRNA*** interaction and on post-translational modifications of further elucidation of the mechanism of ***mRNA*** degradation of cytokines and proto-oncogenes.

L10 ANSWER 11 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 97316289 EMBASE
DN 1997316289
TI Inhibitor of protein tyrosine kinase, ***radicicol*** , suprresses the expression of cyclooxygenase and pro-inflammatory cytokines in LPS-stimulated rat alveolar macrophage in part by accelerating degradation of ***mRNA*** .
AU Feng L.; Jang B.C.; Hwang D.
CS L. Feng, Department of Immunology, Scripps Research Institute, San Diego, CA 92037, United States
SO Advances in Experimental Medicine and Biology, (1996) 407/- (281-288). Refs: 24
ISSN: 0065-2598 CODEN: AEMBAP
CY United States
DT Journal; Conference Article
FS 005 General Pathology and Pathological Anatomy
LA English
SL English
AB The protein tyrosine kinase inhibitor, ***radicicol*** , inhibits the expression of COX-2, TNFa, and IL-1b in LPS-stimulated rat alveolar macrophages. However, it did not inhibit the expression of the tyrosine phosphatase (3CH134) dephosphorylating MAP kinases. The inhibition of COX-2 expression by ***radicicol*** appears to occur to mainly at post-transcriptional steps. The inhibition of TNFa and IL-1b expression by ***radicicol*** is at least in part due to accelerated decay of ***mRNA*** . ***Radicicol*** also inhibits tyrosine phosphorylation of MAP kinases. However, whether the activation of MAP kinases is required for the expression of COX-2, TNFa, and IL-lb is not known. The proximal step in LPS-induced signaling pathways leading to the expression of COX-2, TNFa, IL-lb and perhaps other immediate early genes contains tyrosine kinase(s) that can be inhibited by ***radicicol*** . One of these upstream tyrosine kinases appears to be p53/56(lyn).

L10 ANSWER 12 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
8
AN 1995:206748 BIOSIS
DN PREV199598221048
TI ***Radicicol*** , a protein tyrosine kinase inhibitor, suppresses the expression of mitogen-inducible cyclooxygenase in macrophages stimulated with lipopolysaccharide and in experimental glomerulonephritis.
AU Chanmugam, Prithiva; Feng, Lili; Liou, Shuenn; Jang, Byeong C.; Boudreau, Mary; Yu, Gan; Lee, Jong H.; Kwon, Ho J.; Beppu, Teruhiko; Yoshida, Minoru; Xia, Yiyang; Wilson, Curtis B.; Hwang, Daniel (1)
CS (1) Pennington Biomed. Res. Cent., Louisiana State Univ., 6400 Perkins Road, Baton Rouge, LA 70808 USA
SO Journal of Biological Chemistry, (1995) Vol. 270, No. 10, pp. 5418-5426.
ISSN: 0021-9258.
DT Article
LA English
AB Two isoforms of cyclooxygenase (COX) have been identified in eukaryotic cells: a constitutively expressed COX-1 and mitogen-inducible COX-2, which is selectively expressed in response to various inflammatory stimuli. Thus, COX-2 instead of COX-1 is implicated to produce prostanoids mediating inflammatory responses. Major efforts have been focused on identifying nonsteroidal anti-inflammatory drugs (NSAIDS) which can selectively inhibit the enzyme activity of COX-2. Such NSAIDS would be more desirable anti-inflammatory agents in comparison to NSAIDS which

inhibit both COX-1 and COX-2. Other than glucocorticoids, pharmacological agents which can selectively suppress the expression of COX-2 without affecting that of COX-1 have not been identified. We report here that ***radicicol*** , a fungal antibiotic, is a potent protein tyrosine kinase inhibitor, and that it inhibits the expression of COX-2 without affecting COX-1 expression in lipopolysaccharide (LPS)-stimulated macrophages with the IC-50 value of 27 nM. ***Radicicol*** inhibited tyrosine phosphorylation of p53/56-lyn, a Src family tyrosine kinase and one of the major tyrosine-phosphorylated proteins in LPS-stimulated macrophages. ***Radicicol*** also inhibited COX-2 expression in vivo in glomeruli of rats with experimental glomerulonephritis induced by the anti-glomerular basement membrane antibodies, in which COX-2 expression is known to be enhanced. The enzyme activity of COX-1 or COX-2 was not affected by ***radicicol*** in macrophages. ***Radicicol*** also suppressed the COX-2 expression induced by IL-1-beta in rat smooth muscle cells. Other protein tyrosine kinase inhibitors suppressed the LPS-induced COX-2 expression in macrophages but at much higher concentrations than needed for ***radicicol*** . ***Radicicol*** did not inhibit the COX-2 expression induced by phorbol 12-myristate 13-acetate in macrophages. These results suggest that the activation of tyrosine-specific protein kinases is the proximal obligatory step in the LPS-induced signal transduction pathway leading to the induction of COX-2 expression in macrophages. The magnitude of the inhibition of COX-2 protein synthesis by ***radicicol*** was much greater than that of the steady state levels of COX-2 ***mRNA*** . These results suggest that ***radicicol*** inhibits COX-2 expression mainly at post-transcriptional steps.

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L1 2057 S MRNA (3A) STABL?
L2 48 S L1 (3A) SEQUENCE?
L3 6 S L2 AND (DEGRAD? OR DECAY?)
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 23 DUP REM L2 (25 DUPLICATES REMOVED)
L6 20 S L5 NOT L4
L7 0 S L1 AND (RADICICOL OR RADICICOL ANALOG A)
L8 358 S (RADICICOL OR RADICICOL ANALOG A)
L9 27 S L8 AND MRNA
L10 12 DUP REM L9 (15 DUPLICATES REMOVED)

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NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
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L1 16 STABL? TRANSFECT? (3A) ADVANTAG?

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L2 6 DUP REM L1 (10 DUPLICATES REMOVED)

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L2 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2001:248777 BIOSIS
DN PREV200100248777
TI Inhibition of coxsackievirus B4 replication in stably transfected cells expressing human MxA protein.
AU Chieux, V.; Chehadeh, W.; Harvey, J.; Haller, O.; Wattre, P.; Hober, D. (1)
CS (1) Laboratoire de Virologie, CHRU, Institut Gernez-Rieux, 59037, Lille Cedex: dhober@chru-lille.fr France
SO Virology, (April 23, 2001) Vol. 283, No. 1, pp. 84-92. print. ISSN: 0042-6822.
DT Article
LA English
SL English
AB Coxsackieviruses B (CVB) (B1-B6), positive-strand RNA viruses, cause a variety of diseases. CVB4 may have a causal role in insulin-dependent diabetes mellitus. IFN-alpha inhibits CVB replication; however, the mechanism is not well known. The interferon-alpha-inducible human MxA protein exerts an antiviral activity against negative-strand RNA viruses and against Semliki Forest virus, a positive-strand RNA virus. To test the antiviral spectrum of MxA against CVB4, we took ***advantage*** of ***stably*** ***transfected*** Vero cells expressing MxA (Vero/MxA) in 98% of cells. Compared with control cells, in Vero/MxA cells, CVB4 yields were dramatically reduced and expression of the VP1 CVB protein analyzed by immunofluorescence was highly restricted. Furthermore, the accumulation of positive- and negative-strand CVB4 RNA was prevented as

shown by in situ hybridization and RT-PCR. These results indicate that the antiviral activity of MxA extends to CVB4 and that its replication cycle is inhibited at an early step in Vero/MxA cells.

L2 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1997:401744 BIOSIS
DN PREV199799700947
TI The hepatitis B virus X gene induces p53-mediated programmed cell death.
AU Chirillo, Paolo; Pagano, Sabrina; Natoli, Gioacchino; Puri, Pier Lorenzo; Burgio, Vito Lelio; Balsano, Clara; Levrero, Massimo (1)
CS (1) Lab. Genetic Expression, Fondazione andrea Cesalpino, Istituto I Clinica Medica, Policlinico Umberto I, Viale del Policlinico 155, 00161 Rome Italy
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 15, pp. 8162-8167. ISSN: 0027-8424.
DT Article
LA English
AB The human hepatitis B virus (HBV) protein pX is a multifunctional regulatory protein that is known to affect both transcription and cell growth. Here we describe induction of apoptosis in NIH 3T3 polyconal cell lines upon stimulation of pX expression from a dexamethasone inducible mouse mammary tumor virus (MMTV)-X expression vector. The effect of long-term pX expression on the cell survival of mouse fibroblasts was confirmed in colony generation assays. This effect is not shared either by the other HBV products and it is c-myc mediated, as shown by the use of a dominant negative deletion mutant of c-myc. pX also sensitize cells to programmed cell death after exposure to DNA damaging agents. Taking ***advantage*** of ***stable*** ***transfectants*** carrying the p53val135 temperature-sensitive allele, we directly demonstrate that induction of apoptosis by pX requires p53. In p53 null mouse embryo fibroblasts pX activates transcription and confers an evident growth advantage without loss of cell viability. Although pX protein was not detectable in the experimental conditions we used, our results indicate that its expression affects both cell growth and cell death control.

L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 1997:258745 CAPLUS
DN 126:312840
TI The CMV enhancer stimulates expression of foreign genes from the human EF-1.alpha. promoter
AU Kobayashi, Masayuki; Tanaka, Akiko; Hayashi, Yokichi; Shimamura, Seiichi
CS Biochemical Research Inst., Morinaga Milk Industry, Co., Ltd., Zama, 228, Japan
SO Analytical Biochemistry (1997), 247(1), 179-181
CODEN: ANBCA2; ISSN: 0003-2697
PB Academic
DT Journal
LA English
AB To express foreign genes in mammalian cells, many elements of expression modules including promoters, enhancers, and polyadenylation signals of mRNA have been isolated. Nevertheless, their combinations have not been examd. well from the viewpoints of efficient gene expression. In this report, we chose the promoter from the human polypeptide chain elongation factor-1.alpha. gene, one of the most potent promoters in a wide range of cell types, and found a combination among these elements that enabled us to achieve a high level of gene expression. We have demonstrated that activity of the EF promoter is potentiated efficiently when combined with the CMV enhancer and the poly(A) signal derived from bGH mRNA. Since the activity of the CEF promoter is resistant to the neg. effect of the neo expression unit, expression vectors contg. the CEF promoter combined with the neo expression unit will be useful to express foreign genes transiently and abundantly in COS cells. This property will also work ***advantageously*** to establish ***stable*** ***transfectants*** expressing the gene of interest at high levels through selection of neomycin resistance.

L2 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1996:113408 BIOSIS
DN PREV199698685543
TI Regulation of GABA-A receptor structure and function by chronic drug treatments in vivo and with stably transfected cells.
AU Klein, Ronald L.; Harris, R. Adron
CS Dep. Pharmacol., Univ. Colorado Health Sci. Cent. Veterans Adm. Med. Cent., 4200 E. 9th Ave., Denver, CO 80262 USA
SO Japanese Journal of Pharmacology, (1996) Vol. 70, No. 1, pp. 1-15. ISSN: 0021-5198.
DT General Review
LA English
AB In this article, we review the use of stably transfected cells to study the regulation of receptor structure and function by chronic drug treatments and compare results from these cells to results obtained from other systems, including neuronal cultures and intact animals. We focus on the gamma-aminobutyric acid type A (GABA-A) receptor complex. Sedative/hypnotic drugs such as benzodiazepines, barbiturates and alcohol that potentiate GABA-A receptor function produce tolerance and dependence. Chronic treatment of GABA-A receptor preparations from brain and neuronal cultures with GABA-A agonists, as well as these other three classes of drugs, results in regulation of several properties of the receptor. Drug treatments may regulate levels of binding sites, allosteric binding interactions, receptor function, levels of receptor subunit mRNA and levels of receptor subunit protein. Some or all of these effects may comprise the molecular mechanisms of tolerance to these GABA-A-modulatory drugs. The use of cells stably transfected with neurotransmitter receptors provides a homogeneous population that can be cultured under controlled conditions. As most preparations contain mixed populations of GABA-A receptor subunits, ***stably*** ***transfected*** cells offer the ***advantage*** of the expression of receptors with a defined subunit composition. We conclude that chronic drug treatments regulate allosteric coupling and function of GABA-A receptors in stably transfected cells. This regulation does not appear to be due to decreases in the expression of alpha-1- or beta-1-receptor subunits or to expression of subunits other than alpha-1, beta-1, gamma-2L. Therefore, it is unlikely to be due to changes in receptor subunit composition and probably represents post-translational changes. The rapid regulation of allosteric coupling and function by drug treatment of the stably transfected cells should provide insights to the mechanisms of coupling between GABA-A and benzodiazepine receptors as well as tolerance and dependence of benzodiazepines and ethanol.

L2 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 1992:241650 BIOSIS
DN BA93:129675
TI HUMAN AND MOUSE MX PROTEINS INHIBIT DIFFERENT STEPS OF THE INFLUENZA VIRUS MULTIPLICATION CYCLE.
AU PAVLOVIC J; HALLER O; STAEHELI P
CS INSTITUTE IMMUNOLOGY VIROLOGY, UNIVERSITY ZURICH, CH-8028 ZURICH, SWITZ.
SO J VIROL, (1992) 66 (4), 2564-2569.
CODEN: JOVIAM. ISSN: 0022-538X.
FS BA; OLD
LA English
AB Human MxA and mouse Mx1 are interferon-induced proteins capable of inhibiting the multiplication of influenza virus. MxA protein is localized in the cytoplasm, whereas Mx1 protein accumulates in the nucleus. Taking ***advantage*** of ***stably*** ***transfected*** cell lines that constitutively express either MxA or Mx1 protein, we examined the steps at which these proteins block influenza A viruses. In infected cells expressing MxA protein, all viral mRNAs synthesized as a result of primary transcription in the nucleus by the virion-associated RNA polymerase accumulated to normal levels. These primary viral transcripts were polyadenylated, were active in directing viral protein synthesis in vitro, and appeared to be efficiently transported to the cell cytoplasm. Yet viral protein synthesis and genome amplification were strongly inhibited, suggesting that MxA protein interfered with either intracytoplasmic transport of viral mRNAs, viral protein synthesis, or translocation of newly synthesized viral proteins to the cell nucleus. However, in infected cells expression Mx1 protein, the concentrations of the longest primary transcripts encoding the three influenza virus polymerase proteins PB1, PB2, and PA were at least 50-fold reduced. Accumulation of the shorter primary transcripts encoding the other viral proteins was also inhibited but to a lesser extent. These results demonstrate that the mouse Mx1 protein interferes with primary transcription of influenza virus in the nucleus, whereas the human MxA protein inhibits a subsequent step that presumably takes place in the cytoplasm of infected cells.

L2 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1992:409997 BIOSIS
DN BA94:73197
TI COUPLED EXPRESSION OF CALCIUM TRANSPORT ATPASE AND A DIHYDROFOLATE REDUCTASE SELECTABLE MARKER IN A MAMMALIAN CELL SYSTEM.
AU HUSSAIN A; LEWIS D; SUMBILLA C; LAI L-C; MELERA P W; INESI G
CS DEP. BIOLOGICAL CHEM., UNIVERSITY MARYLAND SCH. MED., BALTIMORE, MD. 21201.
SO ARCH BIOCHEM BIOPHYS, (1992) 296 (2), 539-546.
CODEN: ABBIA4. ISSN: 0003-9861.
FS BA; OLD
LA English
AB Stable expression of a full-length cDNA encoding chicken fast muscle Ca2+ transport ATPase was obtained in a Chinese hamster lung cell line (DC-3F), using a dual-promoter expression vector (pH.beta.FaCA3) in which the ATPase was cloned downstream of a human .beta.-actin gene promoter, and a mutant dihydrofolate reductase cDNA (A3/DHFR) was cloned downstream of an SV40 promoter-enhancer. Owing to its essentially normal catalytic activity and modest (20-fold) resistance to the antifolate methotrexate (MTX), the A3/DHFR mutant enzyme served as an efficient dominant selection marker in transfected cell populations challenged with MTX and, within a broad range of drug concentrations, allowed subsequent amplification and overexpression of vector sequences. In stable transfectants, the expressed ATPase was targeted to intracellular membranes, and the microsomal fractions from those cells exhibited high rates of Ca2+ transport. In comparative experiments using transient expression in COS1 cells, the level of ATPase per transfected cell was greater, but less than 5% of the transfected population exhibited ATPase expression. Furthermore, we opposed to the stable lines, the transiently expression cells could not be propagated. Overall, the yield of ATPase was 12-16 and 4-6 .mu.g per milligram of microsomal protein in the stable and the transient expression system, respectively. The ***advantages*** of the ***stably*** ***transfected*** cell lines therefore lie in the homogeneity of ATPase

expression and its distribution in cells and microsomes, in the large yield of microsomes obtained by continuous cell propagation, and in the reproducible functional characteristics of the microsomes. Moreover, the microsomes derived from stably transfected cell lines provide a convenient system for studies of Ca2+ transport and ATPase partial reactions, eliminating the need to conduct repetitive transient transfections to obtain sufficient amounts of enzyme for functional studies.

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